REMARKS

Claim Amendments

Claim 1 is amended to recite a non-replicating vector construct. The amendment is supported throughout the specification, for example, at page 24, lines 6-13 and at page 22, lines 18-24. The amendment adds no new matter.

Rejection of Claims 1-5, 12-13, and 26-29 under 35 U.S.C. 103(a)

Claims 1-5, 12-13, and 26-29 stand rejected under 35 U.S.C. 103(a) as being obvious over WO 95/07994 ("Dubensky"), in view of Hu et al. AIDS Res. Hum. Retrovir., Vol. 7(7), 615-620 ("Hu"). Applicants respectfully traverse the rejection.

An obviousness rejection under 35 U.S.C. § 103 is appropriate only when the differences between the claimed invention and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." *In re Dembiczak*, 175 F.3d 994, 50 U.S.P.Q.2d 1614, 1616 (Fed. Cir. 1999); 35 U.S.C. § 103(a). The ultimate determination of whether an invention would have been obvious is a legal conclusion based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) any objective evidence of non-obviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966).

In *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734, 82 USPQ2d 1385, 1391 (2007), the Supreme Court explained, "While the sequence of these questions might be reordered in any particular case, the [*Graham*] factors continue to define the inquiry that

controls." The Court said that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *Id.*

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.

Id. at 1740, 82 USPQ2d at 1396. The operative question in this "functional approach" is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.*

As explained in the Examination Guidelines published in the Federal Register on October 10, 2007, persons skilled in the art must have been motivated to combine individually known prior art elements to achieve the claimed invention:

> The rationale to support a conclusion that the claim would have been obvious is that "a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success." If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art. [72 Fed. Reg. 175 at 57534]

Amended independent claim 1 recites a method for generating an immune response comprising: administering to a warm-blooded animal a vector construct comprising a polynucleotide encoding at least one immunogenic portion of an antigen obtained from an intracellular pathogen, wherein the vector construct is a non-replicating vector, and wherein the vector construct is selected from the group consisting of retroviral vectors, alphavirus vectors, parvovirus vectors, and eukaryotic layered vector

initiation system vectors; and administering to said warm-blooded animal, prior to or subsequent to administration of said vector construct, at least one protein which comprises at least one immunogenic portion of an antigen obtained from said intracellular pathogen, such that an immune response against the intracellular pathogen is generated.

Hu teaches that "immunization by priming with live recombinant [vaccinia] virus and boosting with subunit immunogen may be more effective than immunization by either immunogen alone." Hu, Abstract. Dubensky is cited as teaching "alphavirus vectors or layered eukaryotic vector initiation systems capable of expressing a viral antigen to warm-blooded animals in order to generate an antigen-specific immune response, wherein the viral antigen is derived from HIV or hepatitis." Office Action at page 4, lines 5-10. The Office Action maintains its obviousness rejection over Hu and Dubensky and further asserts that "the skilled artisan would indeed have found it obvious to interchange the alphavirus taught by Dubensky for the vaccinia virus taught by Hu et al." Office Action at page 6, lines 9-11. Applicants respectfully disagree with the Office Action because Dubensky's alphavirus vector is not interchangeable with Hu's live vaccinia virus vector.

Hu teaches a prime-boost method of administration comprising a live recombinant vaccinia virus. Hu, Abstract. A live recombinant vaccinia virus is a replicating viral vector. Amended claim 1 recites a non-replicating vector. These are two fundamentally distinct vectors. A replicating viral vector, such as Hu's live vaccinia virus, upon entry into the cells exponentially replicates. A non-replicating vector does not.

Viral vectors that exponentially replicate result in uncontrolled higher viral titers and also significantly larger quantities of both the expressed antigen as well as vector.

Paielli et al. teach that at least a 100-fold greater amount of viral DNA is detected in animals transfected with a replication-competent vector as compared to animals transfected with the same dose of a replication-defective vector. Paielli teaches:

> Rather surprisingly, the amount of Ad5-CD/TK*rep* viral DNA detected in prostate (Fig. 3A, top) and testes and liver (not shown) was at least 100-fold greater than that with the same dose of the replication-defective Ad5-FGNR virus. Whereas 100% of the Ad5-CD/TK*rep*-injected mice contained approximately 1 viral copy/cell in prostate at the Day 8 and 29 time points, Ad5-FGNR-injected animals were estimated to contain <0.01 viral copies/cell.

Paielli et al. 2000. Mol. Therapy. 1:3, p. 263-274 (Exhibit 1). Thus, administration of a live replicating viral vector results in over 100 times more vector as compared to administration of a non-replicating viral vector.

A replicating viral vector is a live virus and therefore elicits a cellular and humoral immune response towards not only the expressed antigen but also the virus itself. Hu et al. supports this notion by teaching: "the strong anamnestic response observed only in mice primed with recombinant vaccinia virus most likely was due to the strong cell-mediated immunity generated by immunization with live virus." Hu at page 618, left hand column, lines 27-30. The cited art highlights the fact that an unwanted immune response is generated towards a live replicating vector. It is clear from the literature that the administration of a live replicating viral vector is not interchangeable with the administration of a non-replicating vector because the two vectors have significantly different dosage and immunological characteristics.

Hu tacitly teaches away from the use of a non-replicating vector. Hu teaches advantages of using a replicating viral vector and that a prime-boost regimen

comprising a replicating viral vector is more effective than immunization with either a vector or protein alone. See, for example, Abstract and Tables 1 and 2. After reading Hu, one of skill in the art would not be motivated to use a non-replicating vector with a prime-boost regime because Hu teaches that a live replicating viral vector boosted with a protein is effective. There is nothing within Hu that would lead one of ordinary skill in the art to the method of amended claim 1 because Hu teaches away from using a non-replicating vector.

Neither Hu or Dubensky teaches or suggests performing a prime-boost method with a non-replicating vector. Hu's prime-boost method relies on *in vivo* replication of a live replicating viral vector which is characterized by an uncontrolled viral titer and an unwanted immune response towards the vector itself. Hu provides no suggestion or motivation to use a non-replicating vector in a prime-boost method. In fact, Hu actually teaches away from using a non-replicating vector. Dubensky teaches non-replicating alphaviruses but certainly does not suggest using such vectors in a prime-boost method. Thus, neither Hu or Dubensky provide any motivation to combine non-replicating vectors with a prime-boost method, as claimed.

Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Dated: October 17, 2007
Customer No. 22907

By: 

Dale H. Hoscheit
Registration No. 19,090